REMARKS

Claims 38-39, 42-46, 56 and 59-71 were pending. Upon entry of this amendment, Claims 38-39, 42-46 and 65-109 will be pending.

This application contains fifty-two (52) claims, of which eight (8) are independent claims.

Rejections Under 35 U.S.C. §§ 112

Claims 56 and 59-64 stand rejected under 35 U.S.C. § 112, first paragraph. The Examiner asserts inter alia that the specification, while being enabling for bone metastases, does not reasonably provide enablement for preventing new bone metastases.

Applicants traverse the rejection and request withdrawal of the same.

Without agreeing in any way with the Examiner's assertion, and to expedite prosecution of the application, claims 56 and 59-64 have been cancelled.

Claims 38-39, 42-46, 56 and 59-71 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particulary point out and distinctly claim the subject matter which the applicant regards as the invention. The Examiner asserts in independent claims 38, 56 and 65, it is not clear that the metastases are metastases from prostate cancer.

Applicants traverse the rejection and request withdrawal of the same.

Claims 38, 56 and 65 have been amended to recite that the metastases are metastases from prostate cancer. New claims 72, 78, 84, 91, 98 and 104 also recite this limitation.

Rejections Under 35 U.S.C. §§ 103

Claims 38-39, 42-46, 56 and 59-71 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Winn *et al.* (6,162,927) in view of Yin *et al.* (BIOSIS AN 1999:441578). The Examiner asserts inter alia that Winn discloses the instant compound is an endothelin antagonist, that endothelin is associated with prostate cancer, and that although the independent claims differ over Winn in reciting inhibiting and preventing bone metastases, Yin discloses that tumor-produced endothelin-1 mediates new bone formation.

The Examiner further asserts that it would be obvious to use anticancer drugs and radiation because the recited treatments are well-known in the cancer art and because the use of more than one drug and radiation is common in the cancer art.

The Examiner still further asserts that it would also be obvious to use an agent that impeded net bone loss since they protect bones from bone turnover that occurs during the formation of osteoblastic bone metastases.

Applicants traverse the rejection and respectfully request withdrawal of the same. For a reference to render the claimed invention unpatentable under 35 U.S.C. 103(a), the cited reference must teach, disclose, or suggest the claimed modification to one of ordinary skill in the art at the time of the invention.

The Examiner is correct in their assertion that the '927 patent teaches the instant compound having formula (III) is an endothelin antagonist; however, the Examiner is incorrect that the combination of the Winn and Yin references teach, disclose or suggest that the instant compound having formula (III) would be useful for treating bone metastases from prostate cancer in a human, as recited in the instant claims. Applicants assert that the combination of these two references would merely teach that the instant compound having formula (III) would be useful in a study of the relationship between Endothelin-1 antagonism and osteoblastic bone metastases from some prostate cancer cell lines in mice calvariae.

Accordingly, the recitation of use of anticancer drugs and radiation therapy during treatment of bone metastases from prostate cancer in a human, defined in the dependent claims, is nonobvious in view of the fact that such treatment is, as written, consonant with the practice of an inventive method of treatment.

Also, treatment with an agent which impedes net bone loss, as defined in the dependent claims, is nonobvious in view of the fact that such treatment is, as written, consonant with the practice of an inventive method of treatment.

CONCLUSION

Entry of the proposed amendment and allowance of Claims 38-39, 42-46 and 65-109 is respectfully requested.

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